BW THREAT REDUCTION MEDICAL PROPHYLAXIS IN THE CZECH REPUBLC

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AIM OF THE PRESENTATION

- Medical response to BW threat
- Preexposure and postexposure medical prophylaxis
- Czech vaccination policy

Medical Response to BW Threat

BW threat
Who are 1st Responders?

- Primary Care Personnel
- Hospital Staff
- EMS Personnel
- Public Health Professionals
- Other Emergency Preparedness Personnel
- Laboratory Personnel
- Law Enforcement

MEDICAL RESPONSE

- **Pre - exposure period**
  - **surveillance system (to monitor unusual illnesses or outbreaks of disease)**
  - **detection, identification of threat / use**
  - **chemoprophylaxis**
  - **immunization**
  - **education**

Diference must be made between

- detection of biological agents in the environment (detection, monitoring)
- medical diagnostics (detection of B- agents, components of agents, or antibodies to B-agents in tissue samples – blood,body fluids)

MEDICAL RESPONSE

- **Post – exposure period**
  - – incubation period
    - active and pasive immunization
    - antimicrobial or supportive therapy
    - isolation precaution
      - – observation, quarantine, ROM
  - – disease onset period
    - diagnosis
    - treatment
    - direct patient care

Pre-exposure and Post-exposure Medical Prophylaxis

The main goal:
Minimize potential impact of BW

PRE-EXPOSURE MEDICAL PROPHYLAXIS

- **Immunoprophylaxis**
  - vaccines against a number of potential BW agents are available
  - many of these vaccines were developed for the protection of laboratory workers or individuals in endemic areas
  - vaccines which are effective under natural circumstances, may not provide a similar degree of protection to people exposed to BA attack
  - vaccines do not immediate protection
- **Chemoprophylaxis**
  - using appropriate drugs offers additional protection
  - must be available for all personel in BW area


LEKARNA
SKLAD LECIV
PRIPRAVNA VIR
SKLAD ZM
SKLADV ZDRAV MATERIALU

POST-EXPOSURE MEDICAL PROPHYLAXIS

- Chemoprophylaxis
  - anthrax (for 60 days)
    - Ciprofloxacin 500 mg PO 2x a day
    - Doxycycline 100 mg PO 2x a day
    - Amoxycilin 500 mg PO 2x a day
  - plaque (7 days)
    - Doxycycline 100 mg PO 2x a day
    - Ciprofloxacin 500 mg PO 2x a day
  - Tularemia (14 days) – Gentamicin, Ciprofloxacin
  - Cholera (7 days)
  - Brucellosis (3 weaks) – ?? Rifampicin, Doxycycline
  - VHF: Ebola, Lassa
    - antivirotics Ribavirin

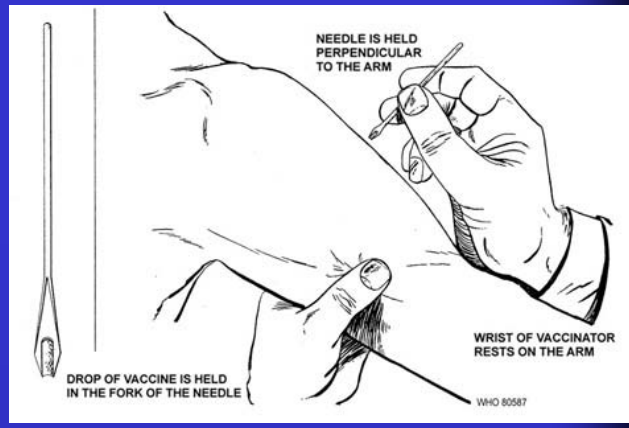
POST-EXPOSURE MEDICAL PROPHYLAXIS

- Active and passive immunization
  - vaccines exist against
    - anthrax
    - smallpox
    - plaque – a killed whole-cell vaccine (pneumonic form ?)
    - tularemia – as investigational new drug in US
    - cholera – DUKORAL, oral live atenuated vaccine, 1 dose
    - Q fever – Q-VAX, formalin killed *C. burnetii,* 1 dose, 5 Y protection
    - VEE – live attenuated vaccine (experimental TC – 83)
    - WEE, EEE – inactivated vaccines
    - botulism – pentavalent toxoid of C.botulinum types A,B,C,D,E
  - vaccines don`t exist against
    - brucellosis,VHF (except Yellow fever), AHF – under development, Ricin, Saxitoxin

SMALLPOX VACCINATION

- Different vaccinia strains have been used for production of vaccine
  - New York City Board of Health (NYCBOH) for US vaccine
    - Dryvax; Aventis Pasteur vaccine
    - newly developed ACAM 1000 (human embryonic lung cell culture) and ACAM 2000 (African green monkey cells – vero cells)
  - live lyophilised Czech vaccine – VARIE + solution VARISOL
    - vaccinia strain used to infect heifer`s skin
    - old vaccine from the 1980`s

VACCINATION



- Intradermal innoculation with bifurcated needle (scarification)
- Vaccinia virus replicates in the dermis of the skin
  - "Major reaction"-
    - Pustular lesion or area of induration surrounding a central lesion (scab or ulcer) 6-8 days after primary vaccination
    - can be misdiagnosed as bacterial superinfection
  - Low grade fever, axillary lymphadenopathy
  - Scar constitutes permanent record of successful vaccination

FIGURE 4. Example of a major reaction (i.e., a take) in a first-time smallpox vaccinee at 6 (left), 10 (middle), and 15 (right) days postvaccination

Source: Reproduced with permission of Stephen P. Heyse, M.D., National Institutes of Health.
Note: Vaccination reactions in vaccinia-naïve and previously vaccinated volunteers in a clinical study of diluted Dryvax® smallpox vaccine; volunteers were enrolled at the NIAID-supported Vaccine Treatment and Evaluation Unit at Saint Louis University in 2002.

VACCINIA CONTACT PRECAUTIONS

- Vaccinia present at lesion from papule (2-5 d) until scabbed (10-19 d p vaccination)
  - lesion covered by dry semipermeable dressing
    - transparent dressings predispose to local secondary innoculation
    - strict handwashing after dressing change
- Vaccinia can be transmitted from a vaccinee`s unhealed vaccination site
  - by close contact
  - can lead to the same adverse events as in the vaccinee
- Excluded from care of vaccinia lesions if pregnant, immunocompromised, or with chronic exfoliative dermatoses

ADVERSE EVENTS

- The frequencies were identified in studies of the 1960s.
- Unknown prevalence of risk factors among today`s population
- Precise predictions of adverse raction rates are unavailable
- Range from mild and self-limited to severe and life-threatening

VACCINIA-COMPLICATIONS

- Normal host
  - Inadvertent innoculation (skin, eye)
  - Generalized vaccinia
  - E. multiforme, urticarial eruptions
  - Postvaccinal encephalopathy, encephalomyelitis
- Pregnancy
  - Fetal vaccinia
- Eczema/exfoliative dermatoses/burns
  - Eczema vaccinatum
- Immunocompromised
  - Vaccinia necrosum

Complication Rates-Vaccinia (Cases per million vaccines)*

Complication	Rate	Complication	Rate
Inadvertent inn.	42	V. necrosum	3
E. multiforme	10	Encephalitis	2
Generalized vacc	9	Other**	39
E. vaccinatum	3	Total	108

* Adapted from Lane et al., *J Infect Dis* 1970;122:303-309

** Incl. bacterial superinfections and lesions uncomfortable enough to result in physician contact. Unusual complications incl. fetal vaccinia, melanoma at vaccine scar, and monoarticular arthritis

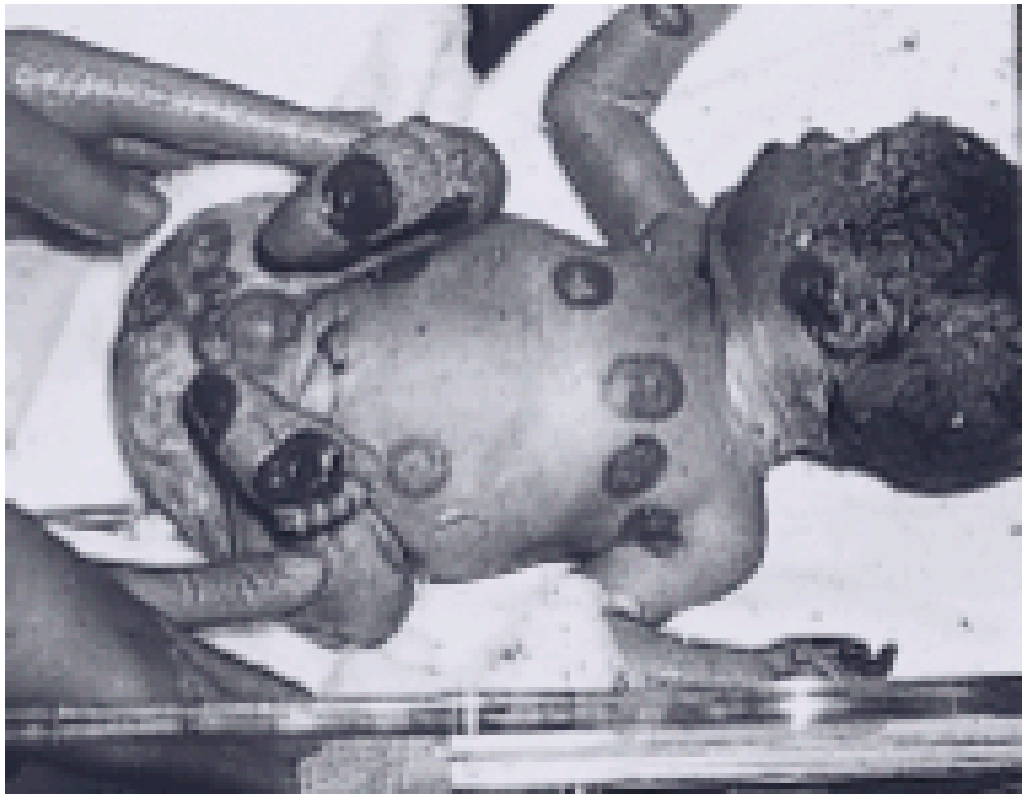
FIGURE 20. Generalized vaccinia with a substantial erythematous base in an infant; note the vaccination site at the left axilla and the apparently well child

Source: Reproduced with permission of J. Michael Lane, M.D.

FIGURE 24. (Top left) A woman aged 22 years with eczema vaccinia acquired from a close contact. She became critically ill, with nearly total involvement of her body, and required thiosemicarbazones, as well as substantial doses of vaccinia immune globulin; (right) side view; (bottom left) residual scarring after resolution of systemic illness

Source: Reproduced with permission of J. Michael Lane, M.D.

FIGURE 33. Fetal vaccinia in a premature infant, 28 week's gestation. Mother received vaccination at 23 week's gestation. The infant died at age 8 days, and vaccinia was isolated from the placenta



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VACCINE CONTRAINDICATIONS

- Immunosupression
  - autoimmune condition, cancer, radiation treatment, immunosuppressive medications
- HIV infection
- History or evidence of eczema
  - possibly other exfoliative or extensive skin lesions-psoriasis, burns
- Pregnancy
- Household/close contacts with above
  - There were no contraindications to vaccinating contacts during era of endemic smallpox

Vaccinia Immune Globulin (VIG)

- Sterile solution of the Ig fraction of plasma with antibodies to vaccinia virus from vaccinated persons
- Must be available to give vaccinia safely, efficacy in the treatment of adverse reactions
- Dose: 0.6 ml/kg IM (can be given at multiple sites/divided doses over 24 -36 hrs)
- VIG aministration is not without risk
- VIG is not recommended for prophylaxis of persons with Smallpox vacc. contraindications
- In Development:
  - IV product
  - Humanized monoclonal antibodies vs epitopes conserved between variola and vaccinia

SMALLPOX: MANAGEMENT OF CONTACTS

- Immediate vaccination (or boosting) of all potential contacts incl. HCWs
  - Clinical “take” within three years confers immunity
  - Most effective if given < 24 hrs p exposure
  - Given within 1 week of exposure can prevent or attenuate disease
- Pregnancy, dermatoses
  - Vaccine + VIG Vaccinia immune globulin (VIG) 0.6 ml/kg IM
    - VIG given using multiple doses/sites/24-36 hrs
- Immunocompromised
  - VIG

CHEMOPROPHYLAXIS

- Chemoprophylaxis no longer available
- Methisazone (Marboran, Burroughs Wellcome)
  - Decreased morbidity and mortality when given to susceptible contacts
  - Limiting side effects: GI intolerance
  - No longer manufactured-not available
- Cidofovir
  - Active in vitro vs variola
  - Active in vivo: postexposure prophylaxis, monkeypox model (rhesus macaques)

Czech Vaccination Policy

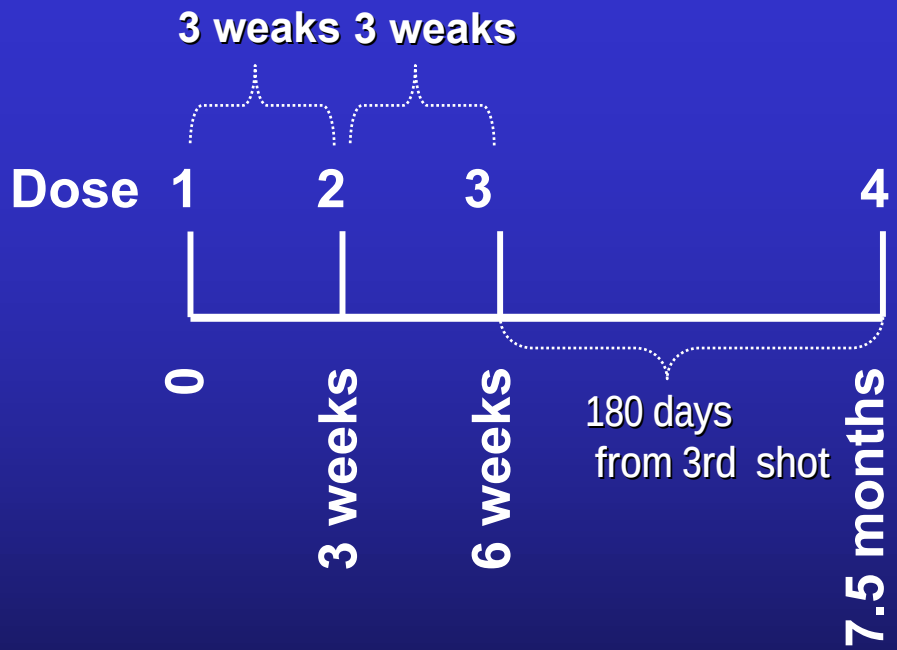
CZECH VACCINATION POLICY

- Civilian and military stockpile of Smallpox vaccines
- Only military stockpile of Anthrax vaccines
- Smallpox vaccination - when and who?
  - only in case of infection apparation as postexposure vaccination
  - for civilian and military people
- Anthrax vaccination – when and who?
  - before unit deployment in risk areas (abroad mission)
  - only military personal

ANTHRAX VACCINATION IN THE CZECH ARMY

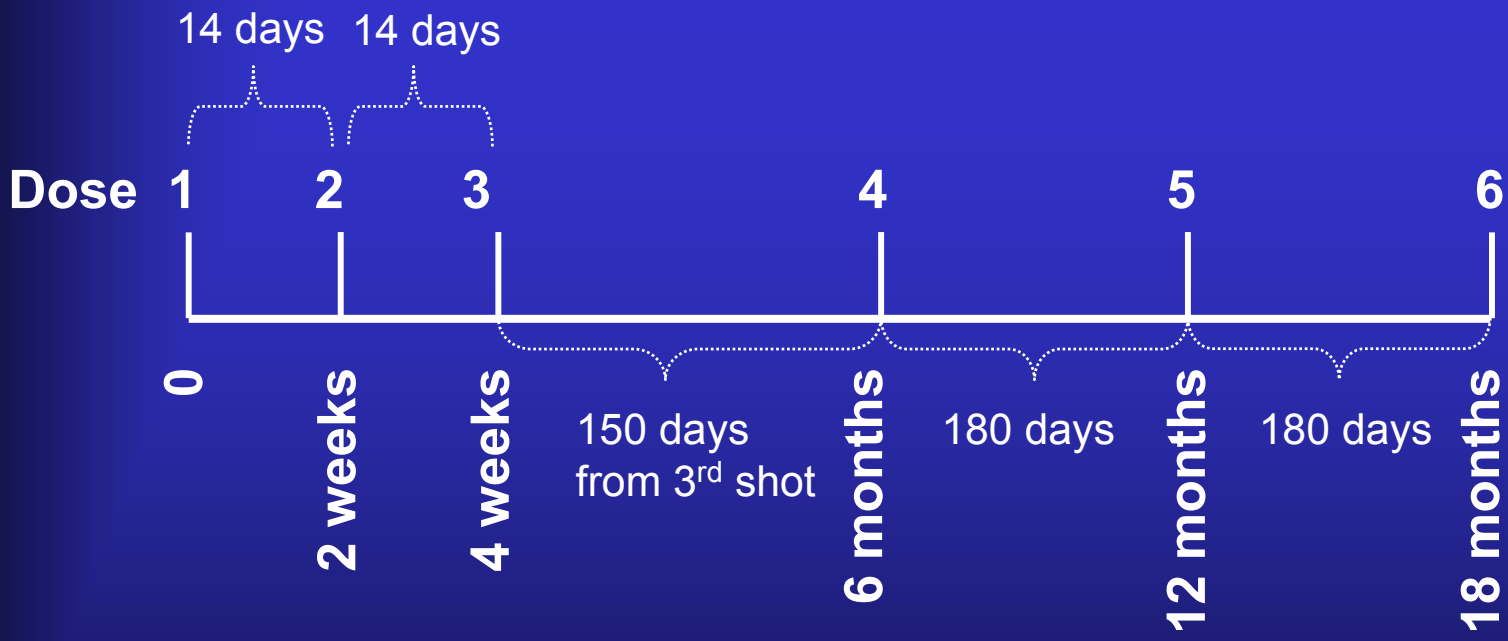
- Anthrax Vaccine
  - produced by MRA/CAMR, Porton Down,Salisbury, UK
  - anthrax antigen + potassium – aluminium sulphate, thiomersal, sodium chlorid,aqua
- Volume: 0.5 ml
- Administration: i.m.
- Booster: 0.5 ml every year

CZECH VACCINE SCHEDULE



- **Four shots over 7.5 months, plus annual boosters**

US Vaccine Schedule



- Six shots over 18 months, plus annual boosters
- Do not compress the schedule
- Adjust schedule for individual delays

ADVERSE REACTIONS

- Approx. 353 vaccinees; 4 refused vaccination
- No clinical trial, only approximated data
  - local reactions – the most common reactions – pain, redness
  - systematic reactions – headache, myalgia, arthralgia, fatigue, fever up to 38° C
- 25 vaccinees found medical advice
  - 8 vaccinees had operating incapacity
- Persisting for 3-4 days
- Anaphylaxis reaction was not reported

SUMMARY

- **Medical prophylaxis** can minimize impact of BW threats
- **Vaccination** is the only practical means of providing continuous protection against BW threats prior to, as well as during, hostile actions
- Initiation of **chemoprophylaxis** during the incubation period is always helpful however the earlier the ATB is given the greater is the change of preventing disease
- The **combined use** of medical countermeasures, physical protection, warning, detection and hazard management provides the basis of defence

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